PTEN knockout prostate cancer as a model for experimental immunotherapy.

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Public Summary:
The PTEN knockout model serves as a highly useful model in which to investigate tumor cell vaccination and adoptive immunotherapeutic strategies in the context of true adenocarcinoma of the prostate. This model should accelerate efforts to develop effective immunotherapies for human prostate cancer.

Scientific Abstract:
PURPOSE: Testing immunotherapeutic strategies for prostate cancer has been impeded by the lack of relevant tumor models in immunocompetent animals. This opportunity is now provided by the recent development of prostate specific PTEN knockout mice, which show spontaneous development of true adenocarcinoma arising from prostate epithelium and more faithfully recapitulate the human disease than any previous model. We investigated the feasibility of using tumor cells derived from this model to test tumor vaccination and adoptive immunotherapeutic strategies for prostate cancer. MATERIALS AND METHODS: PTEN-CaP8 adenocarcinoma cells derived from the biallelic PTEN knockout prostate cancer model were used to vaccinate nontumor bearing litter mates. Tumor specific effector cells were generated from splenocytes of vaccinated mice by mixed lymphocyte-tumor reactions, and antiproliferative effects and cytokine generation were examined in vitro. The effect of vaccination or adoptive immunotherapy on luciferase marked PTEN-CaP8 subcutaneous tumors was monitored by tumor volumetric measurements and noninvasive bioluminescence imaging. RESULTS: Vaccination of litter mate mice with irradiated PTEN-CaP8 cells showed a significant prophylactic effect against the subsequent tumor challenge. Effector cells harvested from vaccinated litter mates showed significant interferon-gamma secretion upon co-incubation with PTEN-CaP8 target cells and they were capable of efficient target cell growth inhibition in vitro. Intratumor adoptive transfer of effector cells resulted in significant growth inhibition of preestablished prostate tumors in vivo. CONCLUSIONS: The PTEN knockout model serves as a highly useful model in which to investigate tumor cell vaccination and adoptive immunotherapeutic strategies in the context of true adenocarcinoma of the prostate. This model should accelerate efforts to develop effective immunotherapies for human prostate cancer.